

### AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the following Listing of Claims.

#### Listing of Claims:

1. (currently amended) An isolated polynucleotide encoding a variant human cytochrome P450 3A4 (CYP3A4)-monooxygenase polypeptide or fragment thereof wherein the polynucleotide is selected from the group consisting of:
  - (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 90;
  - (b) a polynucleotide encoding a polypeptide having comprising the amino acid sequence of SEQ ID NO: 155;
  - (c) a polynucleotide encoding ~~an a~~ CYP3A4-polypeptide, wherein said polynucleotide comprises a sequence corresponding to SEQ ID NO: 90 and comprises a T at the position that corresponds to position 6 of SEQ ID NO: 90;is having at a position corresponding to position 21867 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1) a T,
  - (d) a polynucleotide encoding ~~an a~~ CYP3A4-polypeptide, wherein said polypeptide comprises a sequence corresponding to SEQ ID NO: 155, and comprises an amino acid substitution at the position that corresponds to position 21 of SEQ ID NO: 155at position 363 of the CYP3A4 polypeptide (Accession No: AF280107); and
  - (e) a polynucleotide encoding ~~an a~~ CYP3A4-polypeptide, wherein said polypeptide comprises a sequence corresponding to SEQ ID NO: 155, and comprises an amino acid substitution of T to M at the position that corresponds to position 21 of SEQ ID NO: 155 at position 363 of the CYP3A4 polypeptide (Accession No: AF280107),wherein the polypeptide encoded by the polynucleotide is a variant human cytochrome P450 3A4 monooxygenase polypeptide or fragment thereof, wherein said polypeptide has testosterone or progesterone hydroxylase activity, and wherein said polypeptide has an impaired expression and impaired testosterone or progesterone hydroxylase enzymatic